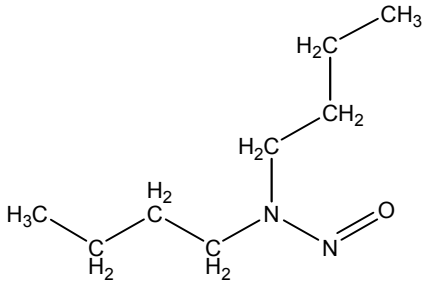
_N_-NITROSODI-_n_-BUTYLAMINE
CAS No. 924-16-3
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

N-Nitrosodi-*n*-butylamine is *reasonably anticipated to be a known human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.4, 1974; IARC V.17, 1978; IARC S.4, 1982; IARC S.7, 1987). When administered orally in the diet, in drinking water, or by stomach tube, *N*-nitrosodi-*n*-butylamine induced papillomas, carcinomas, squamous cell carcinomas, and/or transitional cell carcinomas of the urinary bladder in mice and rats of both sexes, hamsters, and guinea pigs. This compound also caused papillomas, carcinomas, and/or squamous cell carcinomas of the forestomach in male and female mice and male hamsters. *N*-Nitrosodi-*n*-butylamine induced papillomas and/or squamous cell carcinomas of the intestine, esophagus, pharynx, tongue, and soft palate in mice and rats of both sexes; adenomas, papillomas, and/or carcinomas of the trachea, lung, and respiratory tract of male mice and hamsters; and adenomas, carcinomas, and/or cholangiomas of the liver in rats, guinea pigs, and male mice. When injected subcutaneously or intramuscularly, *N*-nitrosodi-*n*-butylamine induced papillomas, carcinomas, and/or hemangiomas of the urinary bladder in mice, rats, hamsters of both sexes, and male rabbits. It also induced papillomas, adenomas, carcinomas, adenocarcinomas, and/or squamous cell carcinomas of the lung, trachea, nasal cavity, and pulmonary system in mice, rats and hamsters of both sexes, and male rabbits. *N*-Nitrosodi-*n*-butylamine also induced squamous cell papillomas, carcinomas, and/or papillomas of the forestomach and esophagus in rats and hamsters of both sexes. This compound caused hepatocellular adenomas and carcinomas in male and female mice, liver carcinomas in rats, mammary carcinomas in female mice, and injection site fibrosarcomas in male hamsters. When administered intraperitoneally, *N*-nitrosodi-*n*-butylamine induced respiratory tract tumors and forestomach papillomas in male and female hamsters. When administered intravenously, this compound caused leukemia in mice of both sexes. When administered transplacentally, *N*-nitrosodi-*n*-butylamine induced respiratory tract tumors in both male and female hamster offspring (IARC V.4, 1974; IARC V.17, 1978).

There is sufficient evidence that the two major metabolites of *N*-nitrosodi-*n*-butylamine, *N*-nitroso-*n*-butyl-*N*-(4-hydroxybutyl)amine (3817-11-6) and *N*-nitroso-*n*-butyl-*N*-(3-carboxypropyl)amine (38252-74-3), are carcinogenic in experimental animals (IARC V.17, 1978). When administered orally in the drinking water, *N*-nitroso-*n*-butyl-*N*-(4-hydroxybutyl)amine induced transitional cell carcinomas, squamous cell carcinomas, undifferentiated carcinomas, carcinosarcomas, and/or papillomas of the urinary bladder in mice and rats of both sexes. It also induced urinary bladder tumors in hamsters. When administered subcutaneously and/or intramuscularly, *N*-nitroso-*n*-butyl-*N*-(4-hydroxybutyl)amine induced urinary bladder carcinomas, respiratory tumors, and cholangiocellular tumors in hamsters. When administered by intravesicular instillation, *N*-nitroso-*n*-butyl-*N*-(4-hydroxybutyl)amine induced

urinary bladder tumors in female rats and bladder carcinomas in dogs. *N*-Nitroso-*n*-butyl-*N*-(3-carboxypropyl)amine, the principal urinary metabolite of *N*-nitrosodi-*n*-butylamine, induced papillomas and transitional cell carcinomas of the urinary bladder in male rats when administered in the drinking water. When administered by intravesicular instillation, *N*-nitroso-*n*-butyl-*N*-(3-carboxypropyl)amine induced urinary bladder tumors in female rats (IARC V.4, 1974; IARC V.17, 1978).

There are no data available to evaluate the carcinogenicity of *N*-nitrosodi-*n*-butylamine in humans (IARC V.17, 1978; IARC S.4, 1982; IARC S.7, 1987). An IARC Working Group reported that the general population may be exposed sporadically to low levels of *N*-nitrosodi-*n*-butylamine; however, no exposed group suitable for an epidemiological study has yet been identified.

PROPERTIES

N-Nitrosodi-*n*-butylamine is a pale yellow oil with a characteristic odor. It is soluble in water and miscible with hexane, dichloromethane, and many other organic solvents. *N*-Nitrosodi-*n*-butylamine is sensitive to light, especially ultraviolet light, and undergoes relatively rapid photolytic degradation. When heated to decomposition, *N*-nitrosodi-*n*-butylamine emits toxic fumes of nitrogen oxides (NO_x).

USE

N-Nitrosodi-*n*-butylamine is used primarily as a research chemical. It has also been used as an intermediate in the synthesis of di-*n*-butylhydrazine, and has been tested for fungistatic activity (IARC V.4, 1974).

PRODUCTION

Current production data are not available. The 1979 TSCA Inventory identified two U.S. companies producing 1,000 lb of *N*-nitrosodi-*n*-butylamine in 1977, but no import or export data were reported (TSCA, 1979).

EXPOSURE

The primary routes of potential human exposure to *N*-nitrosodi-*n*-butylamine are ingestion, inhalation, and dermal contact. The extent of potential human exposure to *N*-nitrosodi-*n*-butylamine during its manufacture is unknown; however, it is prepared in a closed, pressurized process system. Researchers engaged in studying the biological effects of *N*-nitrosodi-*n*-butylamine may possibly be exposed to this compound in the workplace.

N-Nitrosodi-*n*-butylamine has been detected in a variety of products as a result of the nitrosation of amines present in these products. *N*-Nitrosodi-*n*-butylamine is present in soy bean oil at a concentration of 290 µg/kg, in cheese at 20 to 30 µg/kg, and in smoked or cured meats at 0.2-3.9 µg/kg (IARC V.17, 1978). *N*-Nitrosodi-*n*-butylamine has also been detected in tobacco smoke at a concentration of 3 ng/cigarette. It may be present in experimental animal feed at concentrations up to 4.1 µg/kg, and it has been detected in the effluent water from a coke plant at a concentration of 0.82 µg/l. *N*-Nitrosodi-*n*-butylamine may be formed from secondary or

tertiary n-butylamines and quaternary ammonium salts by reaction with nitrosating agents, such as nitrite, in the stomach or during cooking processes. The degree of this potential exposure is unknown, but is assumed to be sporadic and at relatively low levels. Estimates indicate that air, diet, and smoking contribute to potential human exposure at levels of a few µg per day. *N*-Nitrosamines, such as *N*-nitrosodi-*n*-butylamine, are frequently produced during rubber processing and may be present as contaminants in the final rubber product. Potential exposure depends on the ability of the nitrosamine to migrate from the product and enter the body. CPSC and FDA determined that the nitrosamines present in pacifiers and baby bottle nipples can migrate from the pacifier or nipple into saliva, which could result in ingestion of nitrosamines. The computer estimated half-life of *N*-nitrosodi-*n*-butylamine in vapor phase is 2.8 days.

REGULATIONS

EPA regulates *N*-nitrosodi-*n*-butylamine under the Resource Conservation and Recovery Act (RCRA) as a constituent of hazardous waste and under the Clean Water Act (CWA) with respect to hazardous spills. The water quality criteria document for nitrosamines, published under the CWA, includes *N*-nitrosodi-*n*-butylamine. A reportable quantity (RQ) of 10 lb has been established by EPA under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). The Superfund Amendments and Reauthorization Act (SARA) identifies *N*-nitrosodi-*n*-butylamine as a toxic chemical and subjects it to reporting requirements. An enforcement policy was issued by CPSC announcing that the Commission may take action against pacifiers entering interstate commerce that contain more than 60 ppb nitrosamines. FDA has set a 10 ppb limit on nitrosamines in rubber nipples for baby bottles. An American Society of Testing Materials (ASTM) standard has been developed which sets the level of nitrosamines in pacifiers at 10 ppb for any individual nitrosamine. OSHA regulates *N*-nitrosodi-*n*-butylamine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-99.